Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: APD418 (PF-07915504)

Protocol Number: APD418-201(C5061001)

Dates of Study: 28 December 2021 to 19 September 2022

Title of this Study: Hemodynamic Effects, Safety, Tolerability, and Pharmacokinetics of APD418

[A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Assess the Hemodynamic Effects, Safety, Tolerability, and Pharmacokinetics of APD418 in Subjects with Heart Failure with Reduced Ejection Fraction]

Date(s) of this Report: 25 Jul 2023

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is heart failure with reduced ejection fraction?

Ejection Fraction is how much blood is pumped out of the left side of the heart each time it beats. When this pumping does not function normally, the heart will no longer eject enough blood into circulation. This is known as heart failure with reduced ejection fraction.

What is APD418?

APD418 has not been approved for use outside of a research study. When the heart is failing it produces certain types of proteins which are thought to reduce normal pumping of the heart. One such protein is the beta-3 adrenergic receptor (β3-AdrR). APD418 may help the heart function better by binding to the β3-AdrR.

What was the purpose of this study?

The main purpose of this study was to determine if giving APD418 to patients having heart failure with reduced ejection fraction, would improve their heart function. APD418 was given through their veins (intravenously).

In this study some participants took APD418, and some took placebo. A placebo does not have any medicine in it, but it looks just like the study medicine.

Researchers wanted to know:

Did the participants taking APD418 have better heart function compared to those who took placebo?

What medical problems did participants have during the study?

What happened during the study?

How was the study done?

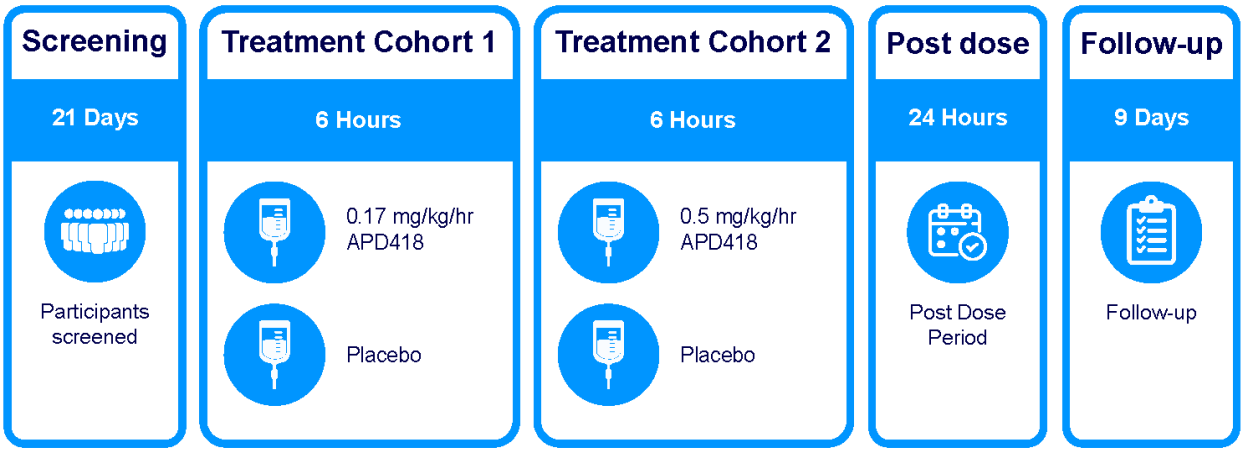
Researchers tested APD418 on a group of study participants to find out if study participants taking APD418 had better heart function when compared to taking placebo.

The participants were divided into 2 groups (Cohorts) as shown in Figure 1.

Group 1: 0.17 mg/kg/hr APD418 (4 participants) or placebo (3 participants)

Group 2: 0.5 mg/kg/hr APD418 (11 participants) or placebo (4 participants)

Figure 1: How was the Study done?



Researchers then compared the results of study participants taking the study medication to the results of study participants taking a placebo medication.

The study participants and researchers did not know who took APD418 and who took the placebo. This is known as a "blinded" study. Study participants were assigned to each group by chance alone.

Where did this study take place?

The Sponsor ran this study in 22 locations in 5 countries; The US, Germany, Poland, Serbia, and Greece.

When did this study take place?

This study began on 28 December 2021, and the Sponsor decided to end the study early, with the study then finishing on 19 September 2022. This was due to a business decision and was not due to any safety concerns about APD418. The Sponsor reviewed the information collected and created a report of the results. This is a summary of that report.

Who participated in this study?

The study included participants who met the inclusion/exclusion criteria for things such as age, condition type, severity, prior treatments etc.

- A total of 17 men and 5 women participated in the study, and all participants (100%) completed study treatment and completed the study.
- All participants were between the ages of 40 and 73.

How long did the study last?

Study participants were in the study for 10 days. The entire study took approximately 9 months to complete.

When the study ended in September 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

Did the participants taking APD418 have better heart function compared to those who took placebo?

Because the Sponsor decided to stop the study early for reasons unrelated to safety, the number of participants was smaller than originally planned and the researchers therefore did not analyse the data as planned. Therefore, the results of the study were inconclusive.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

6 out of 22 participants in this study had at least 1 medical problem. No participants left the study because of medical problems. All common medical problems reported by the participants are described below.

Below are instructions on how to read Table 1

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by the participants are listed.
- The **2nd** column tells how many of the 4 participants taking 0.17 mg/kg/hr APD418 reported each medical problem. Next to this number is the percentage of the 4 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 3 Cohort 1 participants taking a placebo reported each medical problem. Next to this

number is the percentage of the 3 participants taking a placebo who reported the medical problem.

- The **4th** column tells how many of the 11 participants taking 0.5 mg/kg/hr APD418 reported each medical problem. Next to this number is the percentage of the 11 participants taking the study medication who reported the medical problem.
- The **5th** column tells how many of the 4 Cohort 2 participants taking a placebo reported each medical problem. Next to this number is the percentage of the 4 participants taking a placebo who reported the medical problem.
- Using these instructions, you can see that in Cohort 1, 0 out of the 4 (0%) participants taking 0.17 mg/kg/hr reported blood in the urine and a total of 0 out of the 4 (0%) participants taking a placebo reported that blood in the urine. In Cohort 2, 1 out of 11 participants in the 0.5 mg/kg/hr APD418 group and 1 out of 4 participants in the placebo group reported blood in urine.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Cohort 1 0.17 mg/kg/hr APD418 (4 Participants)	Cohort 1 Placebo (3 Participants)	Cohort 2 0.5 mg/kg/hr APD418 (11 Participants)	Cohort-2 Placebo (4 Participants)
Blood in Urine	0 out of 4 participants (0%)	0 out of 3 participants (0%)	1 out of 11 participants (9.1%)	1 out of 4 participants (25%)
Extra Heartbeats	0 out of 4 participants (0%)	0 out of 3 participants (0%)	1 out of 11 participants (9.1%)	0 out of 4 participants (0%)
Tiredness	0 out of 4 participants (0%)	0 out of 3 participants (0%)	1 out of 11 participants (9.1%)	0 out of 4 participants (0%)
Abnormal Level of Heart Failure Biomarker	0 out of 4 participants (0%)	0 out of 3 participants (0%)	1 out of 11 participants (9.1%)	0 out of 4 participants (0%)
Back Pain	0 out of 4 participants (0%)	1 out of 3 participants (33.3%)	0 out of 11 participants (0%)	0 out of 4 participants (0%)

Table 1. Commonly reported medical problems by study participants				
Medical Problem	**Cohort 1** **0.17 mg/kg/hr APD418** **(4 Participants)**	**Cohort 1** **Placebo** **(3 Participants)**	**Cohort 2** **0.5 mg/kg/hr APD418** **(11 Participants)**	**Cohort-2** **Placebo** **(4 Participants)**
Shortness of Breath	0 out of 4 participants (0%)	0 out of 3 participants (0%)	1 out of 11 participants (9.1%)	0 out of 4 participants (0%)
Vein Breakage	1 out of 4 participants (25%)	0 out of 3 participants (0%)	0 out of 11 participants (0%)	0 out of 4 participants (0%)

Did study participants have any serious medical problems?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

No participants in the study had serious medical problems.

No participants died during the study.

Where can I learn more about this study?

If you have questions about the results of your study, please speak with the doctor or staff at your study site.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number APD418-201(C5061001)

The full scientific report of this study is available online at:

www.clinicaltrials.gov	Use the study identifier NCT05139615
www.clinicaltrialsregister.eu	Use the study identifier 2020-006131-10

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for patients.

Again, if you participated in this study, **thank you** for volunteering. We do research to try to find the best ways to help patients, and you helped us to do that!